WEST Search History

DATE: Thursday, October 31, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; THES=ASSIGNEE; PLUR=YES; OP=ADJ			
L3	L1 and ribonuclease	10	L3
L2	L1 and ribonclease	0	L2
L1	l12 and antibody	72	L1

END OF SEARCH HISTORY

09/622,613

Set	Items	Description
S1	261	LL2 AND ANTIBOD?
S2	5	S1 AND RIBONUCLEASE?
S3	2	RD (unique items)
S4	0	ANTI(W)CD22(W)RIBONUCLEASE
S5	5	ANTI(W)CD22(W)TARGETED(W)CYTOTOXIC(W)RIBON?
S6	2	RD (unique items)
S7	265	ONCONASE?
S8	572	LL2
S9	5	S7 AND S8
S10	2	RD (unique items)

Your SELECT statement is:
s l12 and antibod?

Items	File
63	5: Biosis Previews(R)_1969-2002/Oct W2
112	34: SciSearch(R) Cited Ref Sci_1990-2002/Oct W3
6	65: Inside Conferences_1993-2002/Oct W3
19	71: ELSEVIER BIOBASE_1994-2002/Oct W3
42	73: EMBASE_1974-2002/Oct W2
2	94: JICST-EPlus_1985-2002/Aug W3
8	135: NewsRx Weekly Reports_1995-2002/Oct W2
18	144: Pascal_1973-2002/Oct W3
25	149: TGG Health&Wellness DB(SM)_1976-2002/Oct W2
40	155: MEDLINE(R)_1966-2002/Oct W2
14	156: ToxFile_1965-2002/Oct W3
46	159: Cancerlit_1975-2002/Sep
1	162: CAB Health_1983-2002/Sep
1	172: EMBASE Alert_2002/Oct W3
10	266: FEDRIP_2002/Aug
20	399: CA SEARCH(R)_1967-2002/UD=13717
1	442: AMA Journals_1982-2002/Sep B3
2	444: New England Journal of Med._1985-2002/Oct W3

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2002/Oct W2
(c) 2002 BIOSIS
***File 5: Alert feature enhanced for multiple files, duplicates** removal, customized scheduling. See HELP ALERT.
File 34:SciSearch(R) Cited Ref Sci 1990-2002/Oct W3
(c) 2002 Inst for Sci Info
***File 34: Alert feature enhanced for multiple files, duplicates** removal, customized scheduling. See HELP ALERT.
File 155:MEDLINE(R) 1966-2002/Oct W2
***File 155: Alert feature enhanced for multiple files, duplicates** removal, customized scheduling. See HELP ALERT.
File 159:Cancerlit 1975-2002/Sep
(c) format only 2002 Dialog Corporation

3/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12872290 BIOSIS NO.: 200100079439
Interferon resistance of cutaneous T-cell lymphoma-derived clonal T-helper 2 cells allows selective viral replication.
AUTHOR: Dummer Reinhard(a); Dobbeling Udo; Geertsen Ralf; Willers Jorg; Burg Gunter; Pavlovic Jovan
AUTHOR ADDRESS: (a)Department of Dermatology, University Hospital Zurich, Gloriastrasse 31, CH-8091, Zurich: dummer@derm.unizh.ch**Switzerland
JOURNAL: Blood 97 (2):p523-527 January 15, 2001
MEDIUM: print
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Cutaneous T-cell lymphomas (CTCL) comprise a heterogeneous group of lymphoproliferative disorders that are characterized by an accumulation of T-lymphocytes in the skin and occasionally in blood known as Sezary syndrome (SS). In most cases the dominant clone displays T-helper 2 cytokines. Because IFN-gamma is a natural inhibitor of T-helper 2 cells and IFN-alpha is frequently used in CTCL, the impact of IFNs on SS-derived purified clonal T-helper 2 cells was studied using anti-Vbeta **antibodies** . Moreover, IFNs are known to mediate virus resistance in normal cells. The isolated clonal CD4+ cells, but not the nonclonal CD4+ cells, appeared resistant to IFN-gamma and IFN-alpha stimulation in terms of human leukocyte antigen up-regulation and MxA induction caused in part by alterations in Stat-1 molecule mRNA and IFNgammaR1 mRNA transcription. The IFN resistance of the patient-derived

clonal cells was then targeted by vesicular stomatitis virus infection after IFN-alpha priming, resulting in selective viral replication in clonal cells. In contrast, nonclonal cells of the same patient showed IFN-dependent MxA expression, which is a major mediator protein of viral protection. The IFN resistance of the dominant T-helper 2 cells might be important for lymphomagenesis. Interferon signaling deficiencies can be targeted for purging patients' cells in vitro. Furthermore, this approach may allow specific molecular interventions, resulting in the efficient treatment of CTCL and other IFN-resistant neoplasms such as lung cancer.

DESCRIPTORS:
MAJOR CONCEPTS: Integumentary System (Chemical Coordination and Homeostasis); Infection; Hematology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Pharmacology; Blood and Lymphatics (Transport and Circulation); Tumor Biology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Rhabdoviridae (animal host only)--Animal Viruses, Viruses, Microorganisms
ORGANISMS: Daudi cell line (Hominidae); human (Hominidae); mouse (Muridae); vesicular stomatitis virus (Rhabdoviridae (animal host only))
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animal Viruses; Animals; Chordates; Humans; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates; Viruses
DISEASES: Sezary syndrome--blood and lymphatic disease, immune system disease, neoplastic disease; cutaneous T cell lymphoma--blood and lymphatic disease, immune system disease, neoplastic disease; non-Hodgkin's lymphoma
CHEMICALS & BIOCHEMICALS: HLA; IFN-gamma {interferon-gamma}; IFN-gamma-R1 mRNA {Ifn-gamma-R1 messenger RNA}; **LL2** -onconase; T-helper 2 cytokines; anti-CD22-targeted cytotoxic **ribonuclease**
MISCELLANEOUS TERMS: viral replication
ALTERNATE INDEXING: Sezary Syndrome (MeSH); Lymphoma, T-Cell, Cutaneous (MeSH); Lymphoma, Non-Hodgkin (MeSH)

3/9/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12866368 BIOSIS NO.: 200100073517
Potent and specific antitumor effects of an anti-CD22-targeted cytotoxic ribonuclease **: Potential for the treatment of non-Hodgkin lymphoma.**
AUTHOR: Newton Dianne L; Hansen Hans J; Mikulski Stanislaw M; Goldenberg David M; Rybak Susanna M(a)
AUTHOR ADDRESS: (a)NCI-FCRDC, Bldg 567, Rm 162, Frederick, MD, 21702-1201: rybak@ncifcrf.gov**USA
JOURNAL: Blood 97 (2):p528-535 January 15, 2001
MEDIUM: print
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: **LL2** , an anti-CD22 monoclonal **antibody** against B-cell lymphoma, was covalently linked to the amphibian **ribonuclease** , onconase, a member of the pancreatic RNase A superfamily. **LL2** increased in vitro potency (10 000-fold) and specificity against human Daudi Burkitt lymphoma cells while decreasing systemic toxicity of onconase. Monensin further increased potency of **LL2** -onconase on Daudi cells (IC50, 20 and 1.5 pM, absence and presence of monensin, respectively). A 1-hour exposure to **LL2** -onconase was sufficient to kill Daudi cells in culture. These favorable in vitro properties translated to significant antitumor activity against disseminated Daudi lymphoma in mice with severe combined immunodeficiency disease. In mice inoculated with tumor cells intraperitoneally (ip), **LL2** -onconase (100 mug 5 times ip every day) increased the life span of animals with minimal disease 200%. The life span of mice with advanced disseminated Daudi lymphoma (tumor cells inoculated intravenously) was increased 135%. Mice injected with **LL2**

-onconase tolerated a dose as high as 300 mg/kg. Because both onconase and **LL2** are in clinical trials as cancer therapeutics, the covalently linked agents should be considered for treatment of non-Hodgkin lymphoma.

REGISTRY NUMBERS: 11096-26-7: ERYTHROPOIETIN
DESCRIPTORS:
MAJOR CONCEPTS: Endocrine System (Chemical Coordination and Homeostasis); Hematology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Pharmacology; Blood and Lymphatics (Transport and Circulation); Cardiovascular System (Transport and Circulation)
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Daudi cell line (Hominidae); human (Hominidae)--patient; mouse (Muridae)--SCID
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
DISEASES: cardiac dysfunction; erythrocytosis; non-Hodgkin's lymphoma--blood and lymphatic disease, immune system disease, neoplastic disease; premature death; tissue hypoxia
CHEMICALS & BIOCHEMICALS: **LL2** -onconase--antineoplastic-drug, dose tolerability, hematologic-drug, specificity; anti-CD22-targeted cytotoxic **ribonuclease** --antineoplastic-drug, dose tolerability, hematologic-drug, specificity; erythropoietin
MISCELLANEOUS TERMS: blood volume; hematocrit; life span

Your SELECT statement is:
s l12 and antibody

Items	File
56	5: Biosis Previews(R)_1969-2002/Oct W4
107	34: SciSearch(R) Cited Ref Sci_1990-2002/Oct W4
5	65: Inside Conferences_1993-2002/Oct W4
18	71: ELSEVIER BIOBASE_1994-2002/Oct W4
42	73: EMBASE_1974-2002/Oct W3
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18	144: Pascal_1973-2002/Oct W4
23	149: TGG Health&Wellness DB(SM)_1976-2002/Oct W3
33	155: MEDLINE(R)_1966-2002/Oct W4
13	156: ToxFile_1965-2002/Oct W4
39	159: Cancerlit_1975-2002/Sep
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17	399: CA SEARCH(R)_1967-2002/UD=13718
1	442: AMA Journals_1982-2002/Oct B2
2	444: New England Journal of Med._1985-2002/Oct W4

15 files have one or more items; file list includes 27 files.

?b 159, 34, 155
30oct02 16:42:40 User264783 Session D211.2
$0.79 0.452 DialUnits File411
$0.79 Estimated cost File411
$0.21 TELNET
$1.00 Estimated cost this search
$1.05 Estimated total session cost 0.616 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 159:Cancerlit 1975-2002/Sep
(c) format only 2002 Dialog Corporation
File 34:SciSearch(R) Cited Ref Sci 1990-2002/Oct W4
(c) 2002 Inst for Sci Info
***File 34: Alert feature enhanced for multiple files, duplicates** removal, customized scheduling. See HELP ALERT.
File 155:MEDLINE(R) 1966-2002/Oct W4
***File 155: Alert feature enhanced for multiple files, duplicates** removal, customized scheduling. See HELP ALERT.
3/9/1 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

02698245 20584593 PMID: 11154233
Potent and specific antitumor effects of an anti-CD22-targeted cytotoxic ribonuclease : potential for the treatment of non-Hodgkin lymphoma.
Newton D L; Hansen H J; Mikulski S M; Goldenberg D M; Rybak S M
SAIC Frederick, National Cancer Institute-Frederick Cancer Research and Development Center, Frederick, MD 21702-1201, USA.
Blood (UNITED STATES) Jan 15 2001, 97 (2) p528-35, ISSN 0006-4971 Journal Code: 7603509
Contract/Grant No.: CA39841; CA; NCI; NO1-CO-56000; CO; NCI
Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS
LL2 , an anti-CD22 monoclonal **antibody** against B-cell lymphoma, was covalently linked to the amphibian **ribonuclease** , onconase, a member of the pancreatic RNase A superfamily. **LL2** increased in vitro potency (10 000-fold) and specificity against human Daudi Burkitt lymphoma cells while decreasing systemic toxicity of onconase. Monensin further increased potency of **LL2** -onconase on Daudi cells (IC(50), 20 and 1.5 pM, absence and presence of monensin, respectively). A 1-hour exposure to **LL2** -onconase was sufficient to kill Daudi cells in culture. These favorable in vitro properties translated to significant antitumor activity against

disseminated Daudi lymphoma in mice with severe combined immunodeficiency disease. In mice inoculated with tumor cells intraperitoneally (ip), **LL2** -onconase (100 &mgr;g 5 times ip every day) increased the life span of animals with minimal disease 200%. The life span of mice with advanced disseminated Daudi lymphoma (tumor cells inoculated intravenously) was increased 135%. Mice injected with **LL2** -onconase tolerated a dose as high as 300 mg/kg. Because both onconase and **LL2** are in clinical trials as cancer therapeutics, the covalently linked agents should be considered for treatment of non-Hodgkin lymphoma.

1) The ribonucleases of this invention are isolated from members of the genus Rana, SEQ ID NO:1 represents the nucleic acid sequence of a ribonuclease isolated from Rana pipiens and the corresponding amino acid is represented by SEQ ID NO:2 (RaPLR1) from page 14 lines 21 to page 15 line 21.

2) SEQ ID NO:6 is the amino acid sequence of RaPLR1 with a methionine at the position 1.

3) SEQ ID NO:4 is the amino acid sequence of RaPLR1 with a leucine at the position 23.

4) SEQ ID NO:8 represents the sequence shown in SEQ ID NO:4 but with a methionine at the position 1.

5) SEQ ID NO:9 represents a protein with the amino acid sequence of SEQ ID NO:8 but with a His tag at the N-terminus.

6) SEQ ID NO:11 represents RAPLR1 with a serine at the N-terminus.

7) SEQ ID NO:13 represents RaPLR1 with a serine at the position 2 and methionine at the position 1.

8) SEQ ID NO:28 is the amino acid sequence of RaPLR1 with the signal peptide at the N-terminus.

9) RaCOR1 is from Rana catesbeiana oocytes and the protein sequence had been known in the art before the effective filing date of this application. But this invention is still directed to encompass RaCOR1.

10) SEQ ID NO:14 represents DNA sequence of RaCORa but modified to use the preferred codons for E. coli.

11) SEQ ID NO:15 is the corresponding amino acid sequence.

12) SEQ ID NO:17 is the samen amino acid sequence as SEQ IDNO:15 but with a methionine at position 1.

13) SEQ ID NO:19 is the amino acid sequence of SEQ ID NO:15 but with leucines substituted for methionine at positions 22 and 57.

14) SEQ ID NO:21 is the same as SEQ ID NO:19 except for a methionine at the position 1.

15) SEQ ID NO:22 is the same as SEQ ID NO:21 except a His tag at the N-terminus.

16)SEQ ID NO:24 represents RaCOR1 but with a serine at the N-terminus.

17)SEQ ID NO:26 is the same as SEQ ID NO:24 except a methionine at position 1.

18)Table I at page 44 says that recombinant Rana pipiens RNAase (Q1S), Is this SEQ ID NO:11?, has RNAase activity.

19)Slight change in amino acid composition of a ribonuclese changes the enzymatic activity of the ribonuclease at page. activity is unpredictable

20)Table II at page 45 says that RecRaPLR1 (SEQ ID NO:2?) and recRAPLR O1S (SEQ ID NO:11?) has cytotoxic activity measured according to Rybak et al (1991, J. Biol. Chem. Vol 266, pages 21202-7). Is this mean then the two ribonucleases used in Table II results were linked to human trasferrin or antibodies to the transferring via sulfide bond?